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Drug-resistant tuberculosis in war and complex emergencies: jeopardising progress towards TB elimination and antimicrobial resistance control – a scoping review and perspective

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ABSTRACT

Introduction Nearly 300 million people globally require humanitarian assistance, primarily due to conflicts and complex emergencies (CE). Modern conflicts are increasingly prolonged, deadly and frequent, severely disrupting health systems and hindering the provision of quality tuberculosis (TB) care. Managing drug-resistant TB (DR-TB) in these settings is particularly challenging. War and post-war conditions could potentially amplify resistance. However, evidence on DR-TB in CE-affected countries remains scarce.

Methods A scoping review, including grey literature and consultation with implementing agencies, was conducted to analyse published experiences worldwide in delivering DR-TB care in CE.

Results The review included 16 peer-reviewed articles and 11 reports. Countries affected by war exhibit multiple risk factors for amplifying TB resistance. DR-TB management in CE is ongoing, yet diagnostic access is limited, with notification rates below 20% of estimated cases. Treatment success rates among those diagnosed are comparable to global averages. Innovative approaches, such as molecular tests, shorter regimens and patient-centred approaches, have achieved higher success rates. Information on vulnerable populations, including internally displaced persons, prisoners and children, remains minimal. Only one country had reliable information on DR-TB in prisoners (Iraq), accounting for one-third of the national resistant cohort. Most CE countries rely on external funding for DR-TB programmes.

Conclusions Like in other infectious diseases, war significantly alters DR-TB dynamics in affected countries and bordering or refugee-hosting countries, threatening progress towards TB elimination and exacerbating the global antimicrobial resistance crisis. While innovations have improved the feasibility of DR-TB care in CE, access remains severely constrained. Identified risk factors, challenges and priorities underscore the need for expanded TB support and targeted research, particularly for vulnerable populations in CE scenarios.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ War is a recognised risk factor for antimicrobial resistance. Tuberculosis (TB) is a leading infectious disease in war-affected countries, where morbidity and mortality rates often double or triple, potentially intensifying resistance patterns. Understanding the connections between conflict and resistance is critical for an effective global TB response. Despite some isolated published experiences, there are no specific guidelines or systematic reviews that comprehensively assess the burden, links and consequences of drug-resistant TB (DR-TB) in countries impacted by war or complex emergencies (CE).

WHAT THIS STUDY ADDS

⇒ War is associated with numerous risk factors that amplify DR-TB. Countries in conflict face significant barriers to providing effective DR-TB care, including limited diagnostic access and treatment capacity. However, using advanced diagnostic tools and shorter regimens in supported programmes has demonstrated promising treatment success rates, even in challenging settings. This study identifies high-risk populations and outlines priority interventions to address the rise of DR-TB.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides a foundational evidence base to inform future research and the development of guidelines in this neglected area of public health. It emphasises the urgent need to prioritise TB and DR-TB as a critical health issue, particularly in protracted conflicts, and advocates for its inclusion among other health priorities in CE.

INTRODUCTION

Tuberculosis (TB) remains the leading cause of death from infectious diseases and has consistently ranked among the top ten global causes of death for over a century, briefly overtaken by COVID-19.[1] The pandemic, combined with ongoing conflicts in Europe, Africa and the Middle East, besides socioeconomic inequalities, has reversed years of progress towards ending TB. TB is an airborne infectious disease whose transmission is exacerbated by overcrowding, poverty, malnutrition, global travel, limited access to quality care and other social determinants.[2] Drug-resistant TB (DR-TB) is considered a global concern within the broader antimicrobial resistance (AMR) crisis. Resistance to rifampicin (RIF) and isoniazid, the most critical TB medications, is defined as multidrug-resistant TB (MDR-TB).[3 4]

Management of DR-TB is particularly challenging, requiring specialised diagnostic tools and traditionally prolonged regimens (9–24 months) involving toxic drugs, intensive monitoring and significant resources. Diagnosis is even more difficult in specific populations, such as people living with HIV or children. Advances like nucleic acid amplification tests (NAATs), particularly the Xpert MTB/RIF Ultra assay, have significantly improved the detection of RIF resistance. Despite this, DR-TB accounts for 13% of AMR-related deaths worldwide[4] and is one of the four critical priorities of the WHO in the global AMR crisis.[5]

In 2023, the WHO estimated 10.8 million incident TB cases, including 400 000 DR-TB cases. Of these, only 44% received treatment, reflecting incomplete recovery from prepandemic levels. The global treatment success rate (TSR) was 68%.[1] The number of people exposed to DR-TB remains unknown. A systematic review found that war increases the risk of overall TB by up to 20-fold.[6] Conflicts exacerbate nearly all known TB risk factors, such as overcrowding, malnutrition and health system collapse, leading to higher transmission and resistance rates.[6–9] Despite this, the scope and impact of DR-TB in conflict-affected countries remain poorly understood.

War in the 21st century

Complex emergencies (CE) are humanitarian crises in a country, region or society where there is total or considerable authority breakdowns resulting from internal or external conflict and which requires an international response that goes beyond the mandate or capacity of any single agency and/or the ongoing United Nations country programme.[9]

The Uppsala Conflict Data Programme (UCDP) characterises modern conflicts based on intensity (high or low, according to direct deaths from violence), geographical scope, involved parties and nature or cause of the conflict. But the characteristic that most influences societal dynamics is the conflict length.[10] Destructive forces of war, for a long time, can cause devastating effects on the population's health.[11] Protracted conflicts are considered those with greater destruction of the country, regarding their intractability and longevity.[11 12]

Conflicts in the 21st century are increasingly heterogeneous, with prolonged durations being most impactful on societal dynamics.[10] It is estimated that 60% of conflicts resolved in the early 2000s reignited within 5 years.[13] After conflicts, rebuilding basic infrastructures and services like health and education can take decades.

Natural disasters present shorter duration and less impact on the overall health services, attracting more humanitarian assistance than armed conflicts, which impose a heavier burden on infectious diseases due to sustained destruction.[6] The current geopolitical landscape is more volatile than in previous decades, with rising conflicts and fatalities.[10 14] According to the UCDP, the year 2022, with 310 000 estimated deaths, was the most violent in the last three decades since the Rwanda genocide in 1994.[10] The number of active state-based armed conflicts increased by three in 2023, reaching the highest level ever recorded. In 2024, nearly 300 million people required humanitarian assistance due to conflicts and climate emergencies.[13]

International Humanitarian Law, created to limit the effects of armed conflict on populations, is frequently violated in modern conflicts[15–18]; cities are the main battlefields, destroying basic infrastructures and governance systems with frequent weaponisation of healthcare workers (HCWs) and even United Nations agencies.[16] Insecurity, jointly with the destruction of basic commodities (water and sanitation, food security, employment, energy supply, banking, etc) plus the deliberate attacks on public health infrastructure, deaths and attrition of HCWs are factors that multiply the harm of war and exacerbate these crises.[9 16 19] Consequently, by the end of 2024 there are unprecedented mass population movements: 75.9 million internally displaced persons (IDPs) and 37.9 million refugees.[20 21] All these create ideal conditions for TB and drug resistance to proliferate.[2 9]

Wars and infectious diseases

War, famine, plague and death appear together in multiple cultures and traditions, representing the destruction and the end of the world. Beyond symbolic figures, conflicts initially cause peak morbidity and mortality through direct violence. Over time, infectious diseases, often combined with malnutrition, economic crisis, displacement or untreated non-communicable diseases, account for the majority of deaths, which are civilians rather than combatants.[14] See box 1 for a summary of circumstances increasing the burden and severity of communicable and non-communicable diseases in CE.[6 11 22]

Drug-susceptible TB (DS-TB) has historically shown strong links to wars, with documented prevalence spikes during World Wars I and II[23] and recent wars.[24] Many other significant epidemics have been linked to recent wars: cholera and hepatitis in Iraq (2003), Ebola in West Africa (2014), and polio in Gaza (2024) decades after being declared eliminated.[25–27] It is documented that

Box 1 Circumstances that increase the burden and severity of communicable and non-communicable diseases in complex emergencies[6 11 22]

1. Disruption of healthcare services: Conflict can destroy healthcare infrastructure, including hospitals, clinics and medical supply chains. This disruption makes it difficult for individuals to access essential and specialised care.
2. Increased disease burden: The stress, displacement and living conditions associated with conflict can exacerbate chronic diseases and increase the risk of new health problems. For example, inadequate nutrition, exposure to trauma and lack of access to clean water and sanitation facilities can worsen conditions such as diabetes, hypertension and respiratory diseases.
3. Limited access to diagnosis and medicines: Conflict often disrupts the supply chain, leading to shortages and difficulties obtaining essential tools and drugs for managing acute and chronic diseases. Even if medications are available, they may be unaffordable or inaccessible due to importation, inadequate store conditions, transportation barriers or security concerns.
4. Healthcare worker shortages: Conflict can cause healthcare workers to flee affected areas or be injured or killed, leading to shortages of trained medical personnel. This shortage can further strain healthcare systems and limit the capacity to care for chronic diseases.
5. Mental health impact: The stress, trauma and uncertainty of living in conflict zones can exacerbate mental health conditions, including depression and anxiety, which often coexist with chronic physical illnesses. The lack of mental health resources and the stigma surrounding mental health issues can further compound these challenges.
6. Displacement and vulnerability (clinical and social): Conflict-induced displacement forces many individuals to flee their homes, often leading to overcrowded and unsanitary living conditions in refugee camps or informal settlements. Displaced populations, including children and the elderly, are particularly vulnerable to the adverse health effects of chronic diseases due to limited access to healthcare, poor living conditions and disruptions in social support networks.
7. Long-term economic impact: Conflict can have devastating effects on the economy of affected countries, leading to widespread poverty, unemployment and food insecurity. Socioeconomic deprivation can further exacerbate chronic diseases by limiting access to nutritious food, healthcare services and opportunities for disease prevention and management.

conflicts facilitate the spread of overall bacterial resistance through factors like destroyed infrastructure, interrupted diagnostics and medication supply and mobile populations.[28–30]

In TB care, all these unfavourable conditions exist jointly with a lack of qualified human resources and scarce specific TB investment.[4 6 9] There are remaining challenges to diagnose TB in extrapulmonary cases (frequent in children, malnourished or immunosuppressed individuals) or in its early stages, which can be asymptomatic. However, all can transmit the infection to contacts, and these infected people develop TB disease years or decades later.[31] Recent conflicts, such as the reactivated Ukraine-Russia war (2022), have altered DR-TB dynamics locally and across Europe.[32] There are many documented experiences of disproportionate figures of DR-TB among war refugees, migrants and travellers, affecting the DR-TB dynamics in third countries requiring a multinational response.[7 32–38]

Untreated TB cases present a case-fatality ratio beyond 50% and may transmit the infection to 10–15 contacts annually until death or recovery.[39] However, these figures can be even higher in the conditions previously described in CE. The challenges of managing DR-TB during peacetime are amplified by conflict, and DR-TB management has been traditionally excluded from aid interventions in CE due to its complexity and lack of resources. However, poorly implemented TB control programmes increase the risk of resistance amplification, making DR-TB in CE a largely ignored matter with the potential of being a growing global threat. Technological advances, such as NAATs and ultraportable chest X-ray (CXR) devices, may increase the diagnostic capacity in contexts with minimal infrastructure.[40] Until recently, management required 2 years of daily treatment with toxic drugs and injectables. New shorter and effective regimens like the one comprising Bedaquiline, Pretomanid, Linezolid without or with Moxifloxacin (BPaL/BPaLM) for 6–9 months could make programmatic management of DR-TB (PMDT) more attainable even in challenging scenarios.[41]

A 2022 interagency field guide offers support for TB control in refugee camps, including brief recommendations for DR-TB.[42] But refugees are mainly supported in stable countries with uninterrupted health services. There is no DR-TB manual tailored to CE necessities and limitations. This review explores the available literature on managing DR-TB inside CE to identify risk factors, knowledge gaps, successful interventions and priorities for research and policy.

METHODOLOGY

We systematically explored the existence of studies on DR-TB management in CE. Given the scarcity and heterogeneity of available evidence, a scoping review methodology was employed.[43 44] This approach is recommended for examining the implementation of intricate interventions in areas lacking a clear evidence base.

Inclusion and exclusion criteria

The review considered all contents related to DR-TB in CE, including resistance risk factors, epidemiology, diagnosis, treatment, policy implementation and resistance consequences. It included peer-reviewed publications (eg, trials, observational studies, letters and editorials) and reports from agencies managing DR-TB in CE-affected countries.

The inclusion criteria were those studies focusing on DR-TB within CE-affected countries, including populations directly impacted by war or CE, including IDPs, prisoners and other highly vulnerable groups. Excluded studies were those on susceptible TB or research on

refugees or migrants managed in stable host countries, unaffected by war or health system disruption. While such studies may serve as proxies for CE conditions (particularly those on refugees), they reflect the capacities of host countries, rather than the management reality in CE-affected regions. The focus was on assessing the capacity to address DR-TB within countries directly affected by war or CE. Key publications about DR-TB and refugees were used to complement the findings and the perspective. The study protocol was not registered but is available at the online supplemental appendix.

Time frame and language

Peer-reviewed publications from 1 January 2008 (when WHO declared TB resistance a global priority with the publication of emergency DR-TB guidelines[45] to 23 April 2024, were considered. For grey literature, the time frame was restricted to 1 January 2020 to 23 April 2024, for practicality. No language restrictions were applied.

Databases and search terms

Six electronic databases (MEDLINE, ScienceDirect, Embase, Scopus, Google Scholar and Web of Science) were searched using 39 term variations, including "drug-resistant tuberculosis," "TB resistance," "multidrug-resistant TB," "complex emergencies," "war," "conflict" and "crisis," as well as terms related to vulnerable populations (eg, "prison," "internally displaced populations"). A general search was followed by country-specific queries. Specific searches focused on countries experiencing conflicts or prolonged crises from January 2018 to December 2023, based on UCDP data.[10] These included Burkina Faso, Burundi, the Central African Republic, Democratic Republic of Congo, Ethiopia, Mali, Nigeria, South Sudan, Afghanistan, Iraq, Libya, Palestinian Territories, Somalia, Sudan, Syria, Yemen, Armenia, Azerbaijan, Israel, Russia, Ukraine and Myanmar. Conflicts that did not significantly disrupt health systems or civilian populations, such as regional political tensions in border or maritime areas, or issues related to organised crime, were excluded.

To expand the scope, reference lists and key journals were hand-searched. Google Scholar and implementation agencies (eg, WHO, International Committee of the Red Cross, Médecins Sans Frontières and International Organization for Migration (IOM)) were consulted for grey literature. Direct access to internal documents was obtained from IOM and WHO regional offices (Eastern Mediterranean Region [EMRO], EURO, South-East Asia Region [SEARO]). Conference proceedings and abstracts were included only if full texts were available.

Study selection process

Two independent reviewers (IM-R and MR-O, with academic backgrounds and experience in DR-TB in CE) assessed study eligibility based on titles and abstracts. Full texts of eligible studies were observed by both reviewers, independently and in duplicate. For peer-reviewed and grey literature, the major cause of exclusion was including only information on DS-TB management or studies based in countries not affected by CE and the implicit health service disruption. Both reviewers agreed on the final set of publications eligible for inclusion. Disagreements were resolved through discussion with a third reviewer. The search strategy and findings are summarised in figure 1, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[46]

Data extraction, analysis and synthesis

A standardised data extraction form was developed, and relevant information was extracted by one reviewer (IM-R, MR-O, KB, MRTS) and verified independently by a second reviewer (IM-R or MR-O). Extracted data included study characteristics (author, year, country, study design), conflict duration, participant demographics, DR-TB interventions and outcomes. Details on the search strategy and extracted data are presented in the online supplemental appendix.

A thematic framework was used to synthesise findings, highlighting common challenges, successful experiences and key results. A numerical summary using tables and charts, and a qualitative thematic analysis was used to identify factors contributing to successful DR-TB programmes. While scoping reviews do not weigh studies based on design robustness, findings were summarised with an indication of methodological soundness.[43]

The study appendix includes in-depth details on the review protocol, search strategy and data extraction. The synthesis explores the challenges of DR-TB diagnosis, treatment and outcomes in CE. The results are presented descriptively and supplemented with tables. The findings yield priorities and suggestions for future research, policy and practice improvements, complemented by additional published data on AMR, war, DR-TB and vulnerable populations.

RESULTS

Characteristics of included studies

The review identified 2786 citations, with 1644 retrieved from general searches and 1142 from country-specific searches. After removing duplicates and applying inclusion and exclusion criteria, 33 studies were selected for full-text assessment. An additional 213 citations were identified through non-systematic methods, including Google Scholar searches, review of key references and input from implementing agencies, leading to the full-text assessment of 16 reports. Following this process, 27 articles and reports were included, originating from conflict-affected countries (figure 1). Notably, no studies were found addressing DR-TB in the context of climate change or natural disasters.

Among the 16 peer-reviewed articles in the review (table 1), 44% were commentaries or editorials,[47–53] 37% were cohort studies,[54–59] and 19% described national capacities for DR-TB management in post-conflict

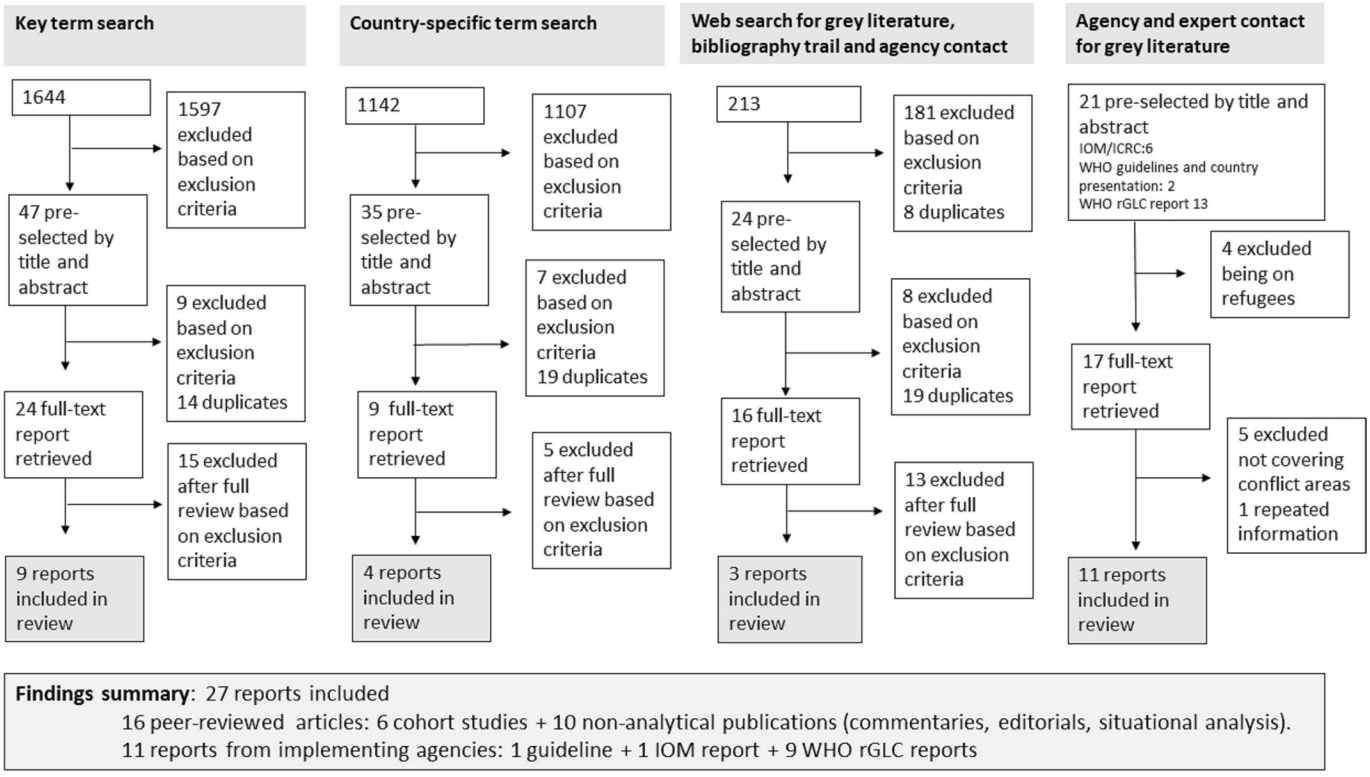

Figure 1 PRISMA flow diagram for systematic reviews. ICRC, International Committee of the Red Cross; IOM, International Organization for Migration; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; rGLC, Regional Green Light Committee.

settings.[60–62] Approximately half of the peer-reviewed articles were related to Médecins Sans Frontières (MSF), and 50% originated from the European region. The most relevant cohort studies, conducted after 2016 and involving more than 150 patients, were from externally supported experiences in three countries: DRC,[55] Afghanistan[56 57] and Iraq.[58] These studies reported TSR above the global average, with one study in Kandahar (Afghanistan) achieving an 89.5% TSR through a shorter regimen and patient-centred care.

The 11 reports selected from implementing agencies (table 2) included one interagency guideline on TB management for refugees,[42] one multicountry report from the IOM,[63] the preliminary data presentation on the BPaLM implementation in Ukraine[64] and detailed WHO reports on DR-TB management in Yemen,[65] Syria,[66] Iraq,[67] Afghanistan,[68] Somalia,[69] Sudan,[70] Myanmar[71] and Ukraine.[72]

These reports provide valuable insights into historical cohorts, laboratory networks, management strategies, logistics and procurement and supply chain management (PSCM). The grey literature offered a broader perspective, complementing the limited peer-reviewed evidence, particularly for the EMRO region and Ukraine, where unpublished successful experiences were documented.

Study results and description of circumstances and interventions

The articles and reports consistently highlighted similar risk factors for TB transmission, disease progression and resistance in CE-affected countries (synthesised in table 3). Overcrowding, malnutrition, weaponising health and educational services leading to health service disruption was a recurrent theme, along with insufficient human resources, centralised services limiting access for remote populations, stigma, economic barriers and the destruction of infrastructure.

Disrupted management of comorbidities, such as HIV/AIDS, hepatitis, malnutrition, other chronic conditions and emotional and physical stress among patients and HCWs, interrupted or challenging logistics, increased in vulnerable populations, limited funds for health activities and overall economic crisis exacerbated these challenges.

Access to quality DR-TB diagnosis was identified as the most critical issue, with notification rates typically between 10% and 20% of the expected incidence. For example, in Myanmar, conflict reactivation in 2021 resulted in a 60% loss of public TB services and a 52% decline in DR-TB notifications compared with 2019.[71]

Mainly, all CE reviewed presented the following characteristics: limited access to quality-assured laboratory services, centralisation of services (large distances between communities and treatment centres), high initial attrition, limited qualified health staff, undernourished patients (eg, 60% in Afghanistan), lack of patient-centred approaches, economic and cultural barriers and TB-related stigma. Where available, fluoroquinolone resistance levels were high among DR-TB patients (eg, 47.6%).[56 57] Studies from Ethiopia[60] and

Table 1 Peer-reviewed findings sorted by WHO regions

	Site and authors	Type of study and population	Type of conflict	Challenges and barriers	Intervention/Results	Proposal/Conclusion
AFRO						
1	Shabunda DRC Shanks *et al* (2012)[54]	Cohort study 3 patients MSF project	Protracted	Collapse of medical services Treatment disruption No access to diagnose	24-month regimen. Simplified protocol for follow-up and monitoring. Education to reduce stigma. MSF support in diagnosis, management and drug procurement	TSR: 100% Management of DR-TB is possible even in remote areas affected by conflict
2	South Kivu DRC Bulabula *et al* (2019)[55]	Cohort Study 1535 patients (DS and DR-TB). TB-REACH grant.	Post-conflict	Destruction of health services Important logistics and structural challenge	Introduction and decentralisation of GeneXpert; RR-TB positivity rate 11%. 9 STR TSR: 83%. 24-month regimen TSR: 74% Predictors of unfavourable outcomes: no DOT, serious adverse drug event	Favourable RR-TB cure rates are achievable. High yield interventions: GeneXpert scale-up; prompt initiation of shorter regimens associated to adherence and socioeconomic support, HCWs training and household-based DR-TB interventions
3	South Sudan Lakshmi (2022)[47]	Correspondence IDPs MSF project	Protracted. High intensity	Priority based on safety and access to water, food Difficulties in access to SLDs	Access to shorter regimens Runaway packs	Maintaining the supply of medication as a fundamental intervention. Use of new short regimens can be an effective option in CE.
4	Ethiopia Gebrehiwot *et al* (2024)[60]	Descriptive study mixed sequential	Active high intensity	Disruption of clinical TB services. Intentional destruction of medical facilities, blockade of essential medicines and security fears. Massive population displacement. Less-impacted medical facilities are unlikely to deal effectively with the sudden surge in demand. No government or agency is able to sustain the TB care.	Loss of more than 75% of TB laboratory diagnostic capacity. From 69 health centres, only 50 kept records. Assistance to TB centres decreased to 34%. Decrease in visits in rural areas. Health facilities systematically looted. Most microscopes and GeneXpert systems were stolen or broken. Death of HCWs. HCWs not receiving wages are forced to be displaced. Disappearance of nearly 90% of ambulances. DR-TB patients' detection was reduced by 49%. Most patient failed to attend their visits during the war.	War resulted in enormous disruption of TB care, requiring urgent restoration. Expected higher mortality, disease prevalence and more severe patterns of disease, including higher rates of DR-TB. Bringing the region back to the prewar level of TB care will take many years and considerable investment.
EMRO						
5	Kandahar, Afghanistan Mesic *et al* (2020)[56]	Cohort study 146 patients MSF project	Protracted	Centralisation (60% of patients not from Kandahar). Lack of qualified laboratories and skilled clinicians. 60% undernutrition. High initial attrition: 23.3%. FQ-R: 47.6%	Use of short regimens Contact tracing Socioeconomic support Laboratory and GeneXpert support Inclusion of Children in DR-TB regimen Flexible approach of the WHO guidelines	High TSR: 79.8% in oral short regimens vs 63.6% with injectable Need for patient patient-centred approach. MSF project.

Continued

Table 1 Continued

	Site and authors	Type of study and population	Type of conflict	Challenges and barriers	Intervention/Results	Proposal/Conclusion
6	Kandahar Afghanistan Mesic *et al* (2022)[57]	Cohort study continuation of cohort another study[56] 236 patients (146 previous and 90 new). MSF project	Protracted	Distances between communities and DR-TB clinics. Limited access to quality-assured laboratory services and qualified health staff. Insecurity. Economic and cultural barriers, TB-related stigma	Patient-centred model. Self-administered vs treatment with monthly drug supplies, family approach and directly observed treatment. Early recognition and management of adverse events. Home visits and intensive adherence counselling. Attributable impact: treatment attrition from 23.3% vs 5.5%, no lost to follow-up during intervention, TSR 74.1% increased to 89.5% (46.3% on short regimens)	Short oral treatment regimens for DR-TB combined with person-centred care can be used as tools to scale up access to care and improve treatment outcomes in CE.
7	Iraq Tesfahun *et al* (2024)[58]	Cohort study 301 patients, (167 with final results). MSF support	Protracted	Centralisation and access to care	Use of short regimens. Support the NTP in data analysis and complex cases.	High TSR: 82.1% in oral short regimens vs 63.3% with injectable LTFU: 2.6% oral vs 17.9% injectable regimens. Need for decentralisation and a patient support package.
EURO						
8	Abkhazia Majumdar *et al* (2011)[48]	Correspondence MSF support	Protracted	An increase in DR-TB since the collapse of the Soviet Union	41% of DR-TB patients had a history of incarceration. Links between conflict/crisis, disruption of health systems and overcrowded and an increase in the imprisoned population.	Scale up of DR-TB from prisons to families and communities. Need for establishment of DR-TB management in prisons and communities.
9	Ukraine Acosta *et al* (2014)[49]	Letter IDPs and refugees	Active high-intensity conflict	Multifactorial increased risk of DR-TB transmission (poor health conditions, overcrowded temporary living conditions)	Thousands of unregistered IDPs without access to medical services in conflict zones: limited access to essential medicines, no service delivery due to ongoing fighting, high risk of treatment interruption, inappropriate regimens and failure and increased patterns of resistance.	Minimum care package for the control of DR-TB. Need for a cross-border legal framework and international collaboration. Expand TB screening programmes for contacts. Increase the availability of DR-TB rapid tests.
10	Ukraine Dudnyk *et al* (2015)[50]	Correspondence	Active high intensity	Nearly 1 M IDPs or refugees. An estimated 3000 DR-TB patients living in affected areas Uninsured drug supplies.	Worst control of DR-TB since the start of the war	Support for education programmes of medical staff and community workers focused on M/XDR-TB must be ensured.
11	Ukraine Kuchuloria *et al* (2016)[51]	Comment	Protracted	Drug supply not guaranteed by the government. Patient paid out of pocket.		Decentralisation. Mobile clinics Unified electronic records. Improved follow-up

Continued

Table 1 Continued

	Site and authors	Type of study and population	Type of conflict	Challenges and barriers	Intervention/Results	Proposal/Conclusion
12	Ukraine Burman *et al* (2018)[52]	Editorial	Protracted	High impact of conflict and economic crisis on HCWs and treatment service delivery. Shortages of medical supplies. Overcrowded hospital facilities. Limited infection control.		Potential increase in DR-TB prevalence. Need for political commitment for finance and international coordination and support for DR-TB control
13	Zhytomyr Oblast Ukraine Gils *et al* (2020)[61]	Cross-sectional on DR-TB service availability survey MSF support	Protracted	Long-term impact of war (2014) in a province not directly affected by it. Lack of specialised DR-TB outpatient facilities. Highly centralised hospitalisation model. Limited adherence support.	Provision of social support, counsel, psychiatric services, ancillary medication and blood tests	Development of outpatient services is fundamental for decentralisation. Multiple needs for an effective transition towards outpatient services with all oral regimen.
14	Ukraine Reames (2023)[62]	PhD thesis, aggregate data and trend analysis	Protracted high intensity	High disruption of medical services, first from the COVID-19 pandemic and then by the highly active conflict.	Significant decrease in DR-TB notifications (from 30% to 18%) in Ukraine from 2020 to 2021. Slight and sustained increase in the last months of 2022.	1. Personnel and resources diverted to immediate medical needs; 2. Personnel burnout: relocation, fleeing or recruiting into the army; 3. Weaponisation of health infrastructure
15	Ukraine Butov *et al* (2023)[53]	Correspondence. National survey on services	Protracted, high intensity	Population displacement. Severe constraints on diagnostic capacities and clinical TB care. Weaponisation of medical services	progressive reduction in the mean number of hospitalised adult TB patients. Shortages of consumables for molecular diagnostics of TB are reported. Several regions experienced stock-outs of other medicines.	TB services have been sustained throughout the territories of Ukraine. Need for continuation of external support for the NTP
WPRO						
16	India Armstrong *et al* (2014)[59]	Cohort study 13 patients	Low-intensity conflict	Undertrained staff. Distances and access to care Lack of qualified laboratories	24-month regimen. Outpatient model based in primary care. Task shifting to non-clinicians, including nurses, with remote support from a TB specialist. Commitment to completion and active follow-up	TSR: 70% of those with final results MSF project

AFRO, Africa; CE, complex emergencies; DRC, Democratic Republic of Congo; DR-TB, dru-resistant TB; EURO, Europe; FQ-R, fluoroquinolone resistance; HCWs, healthcare workers; IDPs, internally displaced populations; LTFU, lost to follow-up; MSF, Médecins Sans Frontières; NTP, National TB Programme; SLDs, second-line drugs; TB, tuberculosis; TSR, treatment success rate.

Ukraine[61] described the impact of war on DR-TB services which included death and fleeing of HCWs, target of civilians and medical facilities, destruction of records and 75% laboratory capacity, blockade of essential medicines, security fears leading to population displacement, limited medical supplies, staff burnout and cessation of critical public services.

Due to security, sanctions and other issues, PSCM of test and medication is a major bottleneck in programme management of DR-TB in CE.[65–70] Stockouts forcing patients to delay diagnosis, enrolment or stop treatments are frequently reported.[65–70] Lack of electricity creates basic problems in diagnosing or properly storing DR-TB drugs with pharmacies operating at >25°C.[65 66]

Even when essential commodities and a steady calm situation are achieved, restored health services frequently collapse due to new conflicts, insecurity and shortage of trained human resources under an entire dependence on external funding.[63 65–72]

In protracted conflicts, long-term planning becomes challenging due to political uncertainties, quickly changing circumstances, reduced inter-agency

Table 2 WHO and IOM report findings

	Report name and type	Summary of key findings, results, interventions and recommendations
1	IOM Middle East response annual report (2022).[63] Narrative report	IOM is the principal recipient of the GF MER (Middle East Response) grant for the MER. Countries included Syria, Jordan, Lebanon, Iraq, Yemen and the Palestinian Territories. Lebanon and Jordan are countries hosting millions of refugees, stressing their TB services and capacities. Syria, Iraq and Yemen, with greatly different circumstances of protracted conflict and instability, share similar challenges in terms of human resources, PSCM and disruption of health services. Despite Iraq's coming out of the emergency, security is still a concern and health services are overcoming long-term challenges. Yemen and Syria remain immersed in unresolved conflict and economic crisis. Details on key challenges, findings and recommendations are included in the online supplemental appendix and consistent with WHO rGLC reports.
2	BPaLM presentation on Ukraine (2024)[64] Presentation of country data under the WHO BPaLM accelerating platform	First registered cohorts of BPaL/BPaLM implementation in CE in a country with a high baseline of DR-TB. Selection of BPaL/BPaLM regimens to improve adherence under crisis and framed in the comprehensive policy of outpatient, primary healthcare and patient-centred. National cohort landmarks: 2020 introduction of BPaLM (171 patients). 2022: BPaL is fully scaled up except in territories in conflict (358 patients). 2023: introduction of BPaLM in the penitentiary system Results: Average TSR: 65%–69% on mSTR vs 89% on BPaLM Cohorts July 2022–January 2023: 1161 RR-TB patients. Of the 358 in BPaL/BPaLM, 318 cured (89.8%) 13 failures (3.7%), 7 deaths (2%), LTFU: 16 (4.5%). Side effects: 352. 9.7% serious side effects, 11.3% needing discontinuation or change and 1.3% full discontinuation Cohort January 2023–March 2024: 4326 RR-TB among those 451 on BPaL and 960 on BPaLM for those with treatment results by March 2024: 88% cured (474 patients), 2.2% failure (12), 5.4% dead (29), 4.3% LTFU (23 patients)
3	Tuberculosis prevention and care among refugees and humanitarian settings Interagency field guide (2022)[42] WHO guideline	Include and recommend DR-TB management (diagnosis, treatment, contact tracing) for all people in need under refugee and humanitarian circumstances based on DR-TB management under the WHO Guidelines 2020. A chapter on DR-TB management, including minimal and comprehensive responses (quick tips and recommendations). Text oriented to refugees, but considering IDPs the most vulnerable to TB due to extreme poverty, overcrowding, malnutrition, poor living conditions, poor access to healthcare and medicines, and frequent LTFU.
4	Yemen WHO rGLC monitoring visit report. (2023)[65] Narrative report	Protracted conflict lasting more than a decade. This fragile state presents one of the greatest humanitarian crises with massive structural challenges. Landmarks: Diagnose 40–45 DR-TB cases per year (12% of expected cases). High Initial Attrition (10%–20%) Sustained TSR close to 70% under challenging circumstances. Introducing new drugs and diagnostic tools (Xpert Ultra and Xpert XDR). Updated DR-TB guidelines. Considering decentralisation and BPaLM introduction Challenges: 4 PMDT sites are understaffed, and no generational relief exists. Low wages. Security concerns. Challenging and delayed PSCM with stock-outs of diagnostic tools and SLDs, creating treatment interruptions, difficult enrolment and limited capacity for M&E, among others. Malnutrition and extreme poverty. No information on IDPs. Full dependency on external financial resources.
5	Syria WHO rGLC monitoring visit report. (2023)[66] Narrative report	Protracted conflict lasting more than a decade. It is one of the greatest humanitarian crises, with massive numbers of refugees and IDPs and major structural challenges like electricity supplies and economic crisis. Landmarks: Diagnoses of 17 DR-TB cases per year (24% of expected cases), an increase in diagnoses. TSR is closed by 70% under challenging circumstances. Introducing new drugs and diagnostic tools (increased GeneXpert network; Xpert Ultra and Xpert XDR). Updated DR-TB guidelines. Challenges: Low wages and high staff turnover. Security concerns. Challenging PSCM with stock-outs of diagnostic tools and SLDs, limited capacity for M&E, among others. Sanctions and border problems limit access to drugs and diagnostic tools—no information on IDPs. Lack of electricity is a core problem for the function of PMDT sites (diagnosis and drug storage). Stigma: No admission of critically ill TB patients in hospitals. No paediatric diagnosis.

Continued

Table 2 Continued

	Report name and type	Summary of key findings, results, interventions and recommendations
6	Iraq WHO rGLC monitoring visit report. (2023).[67] Narrative report	The protracted conflict lasted over a decade, with stability, but civil unrest and insecurity. Landmarks: Continuous decline in estimated TB incidence with increasing treatment coverage and treatment success over time. Notifications from prison and the private sector have increased. The DR-TB network (diagnosis and management) has expanded and is under decentralisation. Five major central prisons provide DR-TB services. BPaL/M started in October 2023. All oral treatment was introduced to detention sites—updated guidelines. Xpert Ultra and Xpert XDR. The NTP expanded access to DR-TB care in 2020 to highly vulnerable groups, including 13 children under 14 years old, 4 pregnant women and patients with comorbidities. Increasing trend of DR-TB notification proportion in imprisoned patients among national cohort: 2019: 5%; 2020: 9%; 2021: 19%; 2022: 27%; 2023: 28%. Around 80% of TB cases among prisoners were discovered by passive case detection, the other 20% is due to active case detection. DR-TB TSR increased from 65% in 2020 to 73% in 2021. Challenges: half of Xpert machines and modules are not functioning; the security situation is unstable and fragile, while poverty, population displacement and social stigma are significant challenges; rapid turnover of trained staff, with TB coordinator shortage in district TB units. Lack of physicians (and/or incentives) willing to work at all levels of TB programme; PSCM is an important bottleneck for PMDT.
7	Afghanistan WHO rGLC monitoring visit report (2023).[68] Narrative report	Protracted conflict, with reactivation and recent conflict stabilisation. Landmarks: 11% increase in diagnosis and 46% in enrolment in DR-TB treatment between 2021 and 2022. Uptake of previous GLC recommendations, including increased children and management of DR-TB contacts. Guidelines are regularly updated (including BPaLM recommendations). 139 machines GeneXpert installed nationwide, including XDR cartridges, decentralised in provincial reference laboratories. Treatment with all-oral regimens (shorter and longer) and available child-friendly formulations. BPaL/M regimen was introduced in all PMDT centres. 10 PMDT sites across 34 provinces, planning decentralisation and ambulatory care. Case finding in IDP: Using digital X-rays was another intervention managed by NTP to identify presumptive TB cases and detect TB cases. UNHCR and IOM support IDP communities. Challenges: There is an 83% gap in DR-TB case detection; the burden is unclear without a DRS survey since 2010. 13% loss to follow-up and 10% died for the 2020 cohort. Delayed GeneXpert cartridge supply. High staff turnover, especially among qualified personnel. Limited or no female staff at PMDT sites
8	Somalia WHO rGLC monitoring visit report. (2023)[69] Narrative report	Protracted conflict lasting more than a decade. Fragile state. Landmarks: 10% and 21% increase in diagnosis and DR TB treatment between 2020 and 2022. Increased laboratory capacity and network for diagnosing and managing DR-TB (73 GeneXperts and XDR cartridges in place). DR-TB TSR: 83% in the 2020 cohort (the highest rate in EMRO). Outpatient management and PMDT expansion (6 functional centres). Guidelines updated based on 2022 WHO recommendations. Implementation of all-oral regimens (shorter and longer). There is no stock of SLDs. Challenges: Undernourishment is a key driver of the TB epidemic in Somalia. Unsustainable partners' support. Suboptimal coordination between states due to security issues and political situations. Limited case finding or contact tracing strategies, challenging access to care due to poor infrastructure for roads and transport, with multiple direct and indirect patient costs, difficult follow-up and adverse reactions management and other multiple complex factors. Full dependency on external financial resources
9	Sudan WHO rGLC monitoring visit report (2023).[70] Narrative report	Protracted conflict with high active reactivation of hostilities. Massive IDP movement, poor TB services coverage in peripheral localities, refugee camps, IDP sites and hard-to-reach areas. Landmarks: 351 microscopy centres and 95 GeneXpert machines providing diagnostic services; In 2021, the DR-TB case notification increased by 36%; Decentralisation of 12 PMDT sites; updated DR-TB guidelines; shorter regimen adopted and implemented Case notification 2021: 210 DR-TB cases out of 1100 estimated cases. Increased diagnosis trend attributed mainly to the GeneXpert scale up since 2017. There was a slight improvement in the enrolment of up to 95% of the detected cases in 2021. TSR 85% in 2020. Challenges: stockout of GeneXpert cartridges in the country, poor and irregular supportive supervision, sputum sample transportation systems, low testing of TB and high LTFU among IDPs and post-conflict areas; high cross-border issues; high staff attrition and presence of demotivated staff; difficult interagency communication. Full external dependence.

Continued

Table 2 Continued

	Report name and type	Summary of key findings, results, interventions and recommendations
10	Ukraine WHO rGLC monitoring visit report (2023).[72] Narrative report	Protracted conflict with high intensity Landmarks: Forced to optimise TB management due to war. Reduction in unnecessary hospitalisation, increase the proportion of outpatient management from 24% in 2021 to 65% in 2023; involvement of primary healthcare providers with a patient-centred approach with VOT Digital Adherence Tools, smart pill boxes, a comprehensive electronic registration tool and enhanced use of technology. Management of comorbidities and mental health, side effect management and palliative care. Expanded services to prisons. Increase access to mWRD platforms (eg, Xpert MTB/RIF or Ultra) and ultraportable CXR assisted by AI. Standardised package of TB community services (non-medical support service) with local/state budget and civil society in communities affected by TB; Food packages and reimbursement of transportation expenses for follow-up and individual needs (documents, clothing, housing…). Unprecedented BPaL/BPaLM scale-up, use of runaway kits (providing long-term supplies of medicines to patients). TSR in non-BPaL/BPaLM regimens: 65%. Training and mentoring to support medical staff Challenges: sample/medication transport, staff burnout, difficulties in screening and contact tracing, infection control and TPT in bunkers, temporary shelters, refugees, IDPs and homeless people. Weaponisation of medical services, laboratories and basic infrastructure. Decrease in general TB notifications, including imprisoned population and DR-TB (decreased by 23 %) Decrease in BCG vaccination coverage. Specific problems in the imprisoned population.
11	Myanmar WHO Joint Program Review of TB 2023.[71] Narrative report	Recent active high-intensity conflict. 1.4 M IDPs, of whom some 1.1 M were displaced by violence since February 2021; UNHCR had estimated the IDP population to have risen to 1.55 million (as of January 2023). Severe disruption of DR-TB services due to security concerns and flee of HCWs. Treatment Services: Not all DR-TB treatment initiation sites were functional due to human resource constraints and location in conflict areas. Service disruptions delayed the uptake of all-oral regimens. Decrease in DR-TB notification and treatment enrolment.

AI, artificial intelligence; BPaL/BPaLM, Bedaquiline, Pretomanid, Linezolid without or with Moxifloxacin; CXR, chest X-ray; DOT, directly observedtherapy ; DR-TB, drug-resistant TB; EMRO, Eastern MediterraneanRegion; HCWs, healthcare workers; IDP, internally displaced population; IOM, International Organization for Migration; LTFU, lost to follow-up; M, million; M&E, monitoring and evaluation ; mWRD, Molecular WHO-recommended rapid diagnostics; M/XDR, multi and extensivelydrug resistant ; NTP, National TB Programme; PMDT, programmatic management of drug-resistant tuberculosis; PSCM, procurement and supply chain management; rGLC, regional Green Light Committee; RR-TB, Rifampicin-resistant tuberculosis; SLDs, second-line drugs; STR, short treatment regimen; TPT, tuberculosis preventive treatment; TSR, treatment success rate; UNHCR, UnitedNations High Commissioner for Refugees; VOT, video observed therapy ; WPRO, Western PacificRegion.

coordination, nearly complete external funding dependence and competition between multiple necessities.[63 65–70] Difficulties in hospital admission were common in Middle Eastern countries due to stigma.

Highly vulnerable populations

Information on DR-TB management in children and IDPs was minimal in published articles, but also in WHO/IOM reports. In CE, these vulnerable groups are not necessarily a minority. Children usually account for 10%–15% of TB cohorts,[73] while IDPs are counted by millions in most countries affected by war. Countries under CE tend to present a high proportion of population imprisoned, overcrowded conditions and limited services where health is not considered a priority.[11] One of the selected studies described the situation in Abkhazia in 2011, after a long-term conflict, where 41% of DR-TB patients had a history of incarceration with a potential DR-TB transmission from prisons into the community.[48] Iraq is the only country in the Middle East reporting a systematic approach to DR-TB in prisons. The proportion of national DR-TB patients who are prisoners rose from 5% in 2019 to 28% in 2023.[67] Information about minorities like LGBTIQ+ individuals, ethnic minorities or others is absent.

Successful interventions

Despite these obstacles, the review identified successful interventions. For the few with access to diagnosis and care in CE, either being on point interventions (eg, MSF projects) or National TB Programme (NTP) data, presented TSR similar to or above the World average; from 70% in Yemen[65] to 83% in Somalia[69] and 89% in Ukraine.[72] According to this review (see tables 1 and 2), the high TSR is probably related to expanded access to CXR and GeneXpert network (Xpert Ultra and XDR cartridges), the use of new drugs and shorter regimens. But selection or even survival bias (related to the barriers to treatment access), the existence of external funding (all peer-reviewed publications received external financing and technical assistance support) or other potential biases may exist. Nonetheless, there is clear progress, as in all revised WHO/IOM reports, countries were moving towards decentralisation, undergoing transition to short all oral regimens (including BPaL/BPaLM regimens) and operating under updated guidelines. In

Table 3 Risk factors for drug-susceptible and drug-resistant TB associated with CE, consequences for DR-TB dynamics and potential support

Risk factor	Circumstances	Consequences of TB epidemic dynamics	Final consequences	Potential support
Overcrowding	Shelter with multiple individuals for days and months. Camps and frequent displacement	Increased exposure to TB and transmission may be greater than the published in normal circumstances	The R0 and reinfection may be greater than that commonly accepted under normal conditions	Early patient recognition and treatment. Contact tracing
Malnutrition (acute, chronic and even mild malnutrition)	Stop trading and finance, creating food insecurity Block of communication and sanctions. No workforce in food generation	Greater chances of TB disease development from infection Greater likelihood of severe disease forms like disseminated TB in low BMI patients	Increased TB incidence and prevalence Increase in TB-related deaths	Nutritional support and TB screening among malnourished adults and children and TB-affected families
Weaponising health and educational services	Infrastructure destroyed. Death of HCWs. Insecurity. Flee and migration of HCWs. No generational relief among TB HCWs	Lower TB notification Lower TB treatment enrolment Lower TB retention Durable disruption of TB services	Greater transmission Increased TB incidence and prevalence Increased TB-related deaths	Accomplishment of International humanitarian law HCWs training Remote support Use of mWRD Task shifting Simplify protocols and STR
Disrupted health services	No delivery of care No human resources No medical supplies or logistics Decreased laboratory capacity Limited NTP capacity	Lower TB diagnoses Lower TB notification Lower treatment enrolment Lower TB retention	Greater transmission (increase in R0) Increased TB incidence and prevalence Increase in deaths Increase of DR-TB	Service reconstruction and renovation Mobile clinics and outpatient services Outreach capacities including runaway kits, VOT, patient training and remote support.
Lack of human-capable resources	Death of HCWs Flee or migration Salaries below living expenses Stress and mental disease Threatened or living under siege Attrition	Lower TB diagnoses Lower TB notification Lower treatment enrolment Lower TB retention	Disruption of health systems Greater transmission, mortality, adherence and DR-TB amplification	External funding Retain human talent Task shifting Simple protocols Training and update
Centralisation of services	Important distance to diagnosis and care centres in settings where travel can be risky	Lower TB diagnoses Lower TB notification Lower treatment enrolment Lower TB retention	Greater transmission (increased R0) Increased TB incidence and prevalence Increased TB-related deaths Increased DR-TB	Decentralisation and sample distribution systems. Outpatient and primary health focus. Training and monitoring. Mobile support and outpatient services. Outreach capacities, runaway kits, VOT, patient training and remote support
Disrupted management of comorbidities (HIV/AIDS, hepatitis, malnutrition, other chronic conditions)	High-HIV-prevalence settings Use of sexual violence Disruption of health services	Increased vulnerability to TB Increased initial patient attrition	Disruption of health systems	Reconstruction of services Training Task shifting

Continued

Table 3 Continued

Risk factor	Circumstances	Consequences of TB epidemic dynamics	Final consequences	Potential support
Emotional and physical stress among patients and HCWs	Violence and siege Future uncertainties Family and friends tragedies Lack of employment Poverty	Greater chances of TB disease development from infection	Increased TB incidence and prevalence	Reconstruction of services Mental health support
Disrupted or challenging logistics	Complicated by security or sanctions Lack of communications Lack of electricity	Inefficient PSCM: no TB drugs No diagnostic capacity	Disruption of health systems Lower TB diagnoses Lower TB notification Lower treatment enrolment Lower TB retention	International PSCM support Shorter regimens Long-life anti-TB formulations, an effective TB vaccine
Increase in vulnerable populations	IDPs: Rampant poverty, housing and food security, forcing the displacement of the population. Increase in the imprisoned population	Increase people exposed Increase overcrowding and transmission Increase clinical susceptibility related to malnutrition and other comorbidities	Greater transmission (increased R0) Increased TB incidence and prevalence Increased TB-related deaths Increased DR-TB	Special focus and services towards care delivery in IDPs and prisoners
Limit funds and economic crisis	Local resources employed in defence and diverted from health and education		Disruption of health services: External dependence	External funding and international support

BMI, body mass index; DR-TB, drug-resistant tuberculosis; IDPs, internally displaced populations; mWRD, molecular WHO-approved rapid diagnostic test; NTP, National TB Programme; PSCM, procurement and supply chain management; R0, The basic reproduction number; expected number of secondary cases produced by a single patient in a completely susceptible population; VOT, video-observed treatment.

the particular case of Ukraine, the country was quickly updating practices like adopting an outpatient model (outpatient from 24% in 2021 to 65% in 2022) with patient centred approach (nutrition, co-morbidities, psycho-emotional support, palliative care), community support (food packages, basic goods, transportation), promotion of short and BPaL/BPaLM regimens and delivering a standardised package of training for primary healthcare mentored by specialists.[64 72] Other flexible approaches had been adapted, like runaway kits (provide patient with ample supplies of medication), maximising technology for diagnosis (molecular platforms, ultraportable CXR assisted by artificial intelligence, etc), mobile phone-based adherence, follow-up and registers application (unified electronic registration tool integrating case management, drug consumption and surveillance).[72]

Regarding BPaLM implementation, the only published information found was a correspondence describing the potential benefits of shorter regimens in IDPs.[47] The preliminary data on the BPaLM implementation in Ukraine, under CE, showed promising results: 89.8% TSR on BPaL/BPaLM cohorts (July 2022–January 2023, 358 patients) in comparison to 65% in the time frame under other regimens. From January 2023 to March 2024, 1411 patients were enrolled in BPaL/BPaLM; for those with treatment results, TSR was 88% (474 patients).[64]

DISCUSSION

War as a risk factor for DR-TB

There is increasing evidence that war and CE create conditions conducive to the spread of MDR bacterial infections.[28 30 74–78] However, despite its significance as one of the four critical pathogens in the AMR crisis,[4] TB resistance is usually not covered even in studies about AMR in refugees.[79] Multiple factors contribute to the increased risk of TB resistance in CE-affected countries, including health system disruption (eg, shortages in diagnostics, drugs and trained personnel), malnutrition, poverty, imprisonment and displacement.[6 9 42 49 51 52] Based on data reviewed, CE-affected countries present multiple of the previous risk factors and challenges already associated with resistance amplification (see table 3) and can be linked to the historical high rates of DR-TB observed in studies among war refugees.[34 35 79–82] More than one precise risk factor, the problem in CE-affected countries is the presence of multiple known DR-TB risk factors, all interacting at the same time. Like in other bacterial diseases, the increase in DR-TB could be considered among the disastrous legacies of war.

Advances in DR-TB management applicable in war settings

Globally, diagnosis remains the weakest component of TB care and control.[4 40] In CE, it was found as the most critical barrier to access to DR-TB care. Early diagnosis

improves outcomes, reduces transmission and enables access to TB preventive therapy.

Molecular testing or NAATs had been successfully introduced in CE. Where available, identifying patients in the early disease stage is less dependent on the operator or sample quality, reducing delays in diagnosis and detecting resistance. The decentralised use of molecular testing NAATs and CXR (with or without AI) under appropriate clinical algorithms may increase the disease presumption and increase diagnostic capacity.

Intensive case finding strategies like patient contacts and relatives (especially children and people living with HIV) done in MSF projects[56 57] added to screening in IDP camps and prisons, like starting to be done in Iraq,[67] could potentially increase the notification rates and identification of TB preventive therapy candidates.[83]

Historically, concerns about resistance amplification had limited the application of DR-TB treatments in CE. In these countries, guidelines[3 4] are mainly applicable in highly centralised settings or with substantial external support. Despite limited published evidence, WHO country reports indicate that programme DR-TB management is expanding in CE. TSRs for patients enrolled in these programmes are similar to global averages. Recent advances in shorter, high-efficacy regimens (6–9 months)[84–87] have reduced treatment costs, although reliance on external funding remains a significant barrier, while health systems need to be strengthened. Patient-centred approaches are essential, but require significant coordination, logistics and human resources. Sustained technical assistance and training showed to have a significant impact on the adoption of new policies and regimens in regional Green Light Committee (rGLC) reports. Linking basic TB approaches with social programmes is often incompatible with the realities of high-intensity conflict phases. Nonetheless, shorter regimens and decentralised care models show promise, even in resource-constrained settings.

The novelties quickly implemented in Ukraine (BPaLM introduction, runaway kits, decentralised diagnosis and management, patient-centred approaches, training for primary healthcare mentored by specialists, maximising technology for PSCM, diagnosis, care and monitoring, etc), could be adapted to other challenging scenarios.

Overlooked vulnerable populations

Modern internal conflicts have displaced millions, with 75.9 million IDPs globally.[20] IDPs face extreme vulnerability due to repeated displacement, rampant poverty, malnutrition, a high proportion of children and limited access to medical care. The lack of data on DR-TB in IDPs suggests either insufficient representation or a lack of access to diagnostic services, making them a neglected high-risk population. Emerging technologies could facilitate targeted screening in IDP camps and shelters.

The risk of DR-TB in prisons is usually disproportionate in countries not affected by conflict.[88] Overcrowding and access to care in prisons are significant challenges in CE. Circumstances are largely unknown except in Iraq, where the proportion of DR-TB patients in prisons rose from 5% in 2019 to 28% in 2023.[67] The situation is concerning, provided that the cases in Iraq come from a pilot initiative limited to a few prisons on passive screening. Similar conditions in prisons were described as the epicentre of the DR-TB epidemic after the collapse of the Soviet Union,[89] while the historical data from Abkhazia showed that 40% of DR-TB cases in the community had a history of incarceration.[48] Future research should consider an intersectional analysis framework, enabling a better understanding of the multiple inequalities affecting access to DR-TB care in vulnerable populations (IDPs, prisoners, children, LGBTIQ+, ethnic minorities and others).

Perspective and priority actions for addressing DR-TB in CE

Although CE shares similar challenges, the nature of each conflict and its effects on populations create heterogeneous conditions. During high-intensity conflict phases, the focus should remain on security, emergency care and basic necessities (food security, water and sanitation, etc). In lower-intensity phases and especially protracted conflicts, TB and DR-TB should be prioritised alongside other key health needs.

Based on the findings, not only new drugs or regimens but also a long-term vision and integrated health system support are critical for DR-TB management in CE. Using the WHO Health System Framework Blocks[90] (table 4), we have synthesised and presented in table 4 the main challenges and priority actions in DR-TB management in CE. As a brief, the key considerations to be strengthened are:

1. PSCM. Needed to assure the availability of diagnostic tools and anti-TB medications. Insecurity, sanctions and heavy border control may delay this process, leading to stockouts and miscalculations.[63 65–70]
2. Security, basic infrastructure and electricity possibilities. These are critical bottlenecks for DR-TB service delivery, such as molecular diagnosis, pharmacies, clinical consultancy, recording and reporting, or distance support. Robust technology and automated low-technical or maintenance-dependent solutions tend to perform longer than delicate or more demanding technology, which usually cannot be fixed or maintained.[63 65–70]
3. Human resource capacities. Local abilities tend to be diminished or outdated after conflicts (deaths, ageing, disability, attrition, education collapse, etc). Re-establishing capacities through external training and technical assistance with task-shifting can be necessary to update, avoid stigma and approach vulnerable populations. Improved staff motivation, team-building and problem-solving skills can be fundamental to retaining talent in NTPs.[63 65–70]
4. Diagnosis networks (including sample transportation), decentralisation and service delivery. To expand diagnosis, consider raising the initial level of presump-

Table 4 Synthesised challenges and priority actions in DR-TB management in CE exposed according to the WHO Health System Blocks framework[90]

(1) Service delivery: deliver effective, safe, quality personal and non-personal health interventions to those that need them, when and where needed, with minimum waste of resources.	
Challenges	Destruction of facilities, weaponising TB services. Centralised services and limited access. Complex diagnosis and clinical management. Low number of capable HCWs. High patient attrition (not starting DR-TB regimens). IDPs, prisoners, children and other highly vulnerable individuals receive minimal DR-TB care.
Priorities and proposed actions	Simpler and less specialised management of DR-TB: Standard management as much as possible, with the remote support of specialists for complex cases or circumstances. User-friendly job aids for quick decision-making. Enhance decentralisation diagnostic capacities: contact tracing+clinical presumption and physical exam+CXR+mWRD. Contact and family screening, putting the focus on children. Secure support and follow-up as much as possible: adherence and early side effect management. Outreach package and model Ensure the treatment enrolment of patients diagnosed. Malnutrition relief: cause and consequences of TB.
(2) Health workforce: works in responsive, fair and efficient ways to achieve the best health outcomes, given available resources and circumstances.	
Challenges	Severe health staff crisis. Poor economies with limited funds for qualified education (ability to increase HCWs) and health financing (limited or no salaries for HCWs). Overwhelmed HCWs need multiple jobs and are likely to suffer stress and mental illness.
Priorities and proposed actions	External funding for rehabilitation and reconstruction. Prevent HCW burnout, retain human talent in countries in conflict and train and develop human resources. Task shift: nurses and community health workers. Highly specialised support is available online or by distance. Field-supportive TA is like the rGLC mechanism or expanded. Training: basic in the early implementation after the high-intensity conflict. Develop and disseminate local capacities.
(3) Health information system: ensures the production, analysis, dissemination and use of reliable and timely information on health determinants, health system performance and health status.	
Challenges	Paper-based usually works. Data will be destroyed during the highly intensive phases. No system for transboundary information on DR-TB.
Priorities and proposed actions	Paper-based or mobile phone-based, simplified versions with minimal data. Transborder information, development of tools.
(4) Medical products: ensure equitable access to essential medical products, vaccines and technologies of assured quality, safety, efficacy and cost-effectiveness, with scientifically sound and cost-effective use.	
Challenges	Stock-outs of critical goods like second-line medication and diagnostic tools (GeneXpert cartridges), international sanctions, quality risks of products due to electricity problems, inefficient management of the PSCM, forecasting, calculation and house maintenance.
Priorities and proposed actions	Adequate PSCM should be the number 1 priority to have at least second-line drugs and mWRD or other TB diagnostic tools Provision of goods: Secure supply of diagnostics and drugs.
(5) Financing: raises adequate health funds to ensure people can use needed services and are protected from financial catastrophe or impoverishment associated with having to pay for them.	
Challenges	Full external dependence. No national wages or below the daily living needs. No funds for TB activities or even drugs. Experiences with inconstant support led to bad outcomes and maybe an increase in the resistance pattern.
Priorities and proposed actions	Given the high level of vulnerability and the consequences of inaction, CE should be a priority for international donors. Long-term commitment and sustainability to a continuum of care. Considering the protracted nature of conflicts, a different way of considering the emergency is needed, considering TB is a leading killer disease in modern conflicts.
(6) Leadership and governance: ensuring the existence of policy frameworks combined with effective oversight, coalition building, regulation, attention to system design and accountability.	
Challenges	Important problems after the war: Lack of government/parliament or difficulties in its formation translated into difficulties in the budget, difficult programming (on a daily basis) and high external dependence even if the country has sources of income. Health leaders can be selected based on political loyalties rather than technical capacities. The high levels of necessity and government (micro or macro) systems based not on merits but on loyalties (past or future) are prone to present high levels of inefficiency and risk of corruption.

Continued

Table 4 Continued

Priorities and proposed actions	Establish DR-TB as a priority in CE as it can ballast country development during ages or decades. Simple guidelines. NSP considers clinical aspects as well as, most importantly, programme aspects. Focus on highly vulnerable populations like IDPs, prison and DR-TB households and malnutrition that require high government coordination.

CE, complex emergencies; CXR, chest X-ray; DR-TB, drug-resistant TB; HCWs, healthcare workers; IDPs, internally displaced populations; mWRD, molecular WHO-approved rapid diagnostic test; NSP, national strategic plan; PSCM, procurement and supply chain management; rGLC, regional Green Light Committee; TA, technical assistance; TB, tuberculosis.

tion with clinical assessment focused on TB, contact tracing and using CXR and molecular tests under decentralised models.[40 55 57 67] Patient-centred models, including nutritional support,[91 92] short regimens and active case finding in households,[40] can be financially challenging but were the most efficient combination found in the review.[57]

5. Focus on vulnerable populations. High-risk and vulnerable populations such as incarcerated individuals, IDPs, minorities and others may hold the biggest burden of DR-TB in CE-affected countries. Focus and prioritise them, may increase the yield and impact of the interventions.[58 67 89 93–96] These groups often experience conditions that facilitate DR-TB transmission and poor treatment outcomes, including overcrowding, limited access to healthcare, malnutrition and interrupted treatment services. Targeted interventions in these 'hot-spot' populations are essential to interrupt transmission chain, ensure early detection and initiation of effective therapy, and reduce health disparities. Tailoring services to these settings is a critical component of an equitable and effective DR-TB response.

Donors and sustainability

The role of donors in sustaining the management of DR-TB in CE was found to be critical in all texts reviewed, where NTPs are fragmented and underfunded.

Sustainability intervention and strategies for transitioning to greater local ownership, like training, field technical assistance and distant/online support, were found beneficial at all rGLC monitoring reports. However, the weaponisation of health services, the disrupted economies and HCW attrition make these needs not as punctual, but long-term interventions depending on the nature and length of the conflict and post-conflict circumstances.

For long-term impact, donor support should be aligned with a sustainability framework that strengthens local capacity, uses new technology and policies, fosters health workforce retention and progressively shifts technical and financial ownership to national programmes, ensuring resilience and self-sufficiency even after external funding declines.

The cost of inaction can be particularly high, leading to increased mortality, ongoing transmission and an impact on the global AMR crisis.

Study limitations

The nature of CE introduces significant challenges to research, including severe understaffing, competing priorities (assistance work) and limited time and research capacity in affected countries. The number and quality of publications was extraordinarily limited, considering that DR-TB management is a common practice in CE.

These factors likely contribute to publication bias, as many critical findings remain undocumented. To address this, a scoping review approach was chosen; however, this methodology has inherent limitations.[44]

The peer-reviewed evidence was limited and heterogeneous, with a substantial proportion of publications comprising editorials and letters. Many of these studies focused on MSF-led projects, which, while pioneering in DR-TB management, may not fully represent the broader reality in CE-affected countries. Additionally, European conflicts were overrepresented in the peer-reviewed evidence, while Middle Eastern countries dominated the findings from WHO and IOM reports. There was a notable lack of access to information from critical CE-affected regions, such as parts of Africa, Latin America and Russia. All these circumstances prevented comparison between world regions in terms of key aspects like diagnostic access, therapeutic coverage and reliance on external funding.

Furthermore, IOM and WHO reports were primarily based on government-provided data, which may be subject to bias, particularly in contexts where governments are directly involved in the conflict.

Successful experiences reported in Ukraine or MSF-led projects may not be fully generalisable to other CE settings due to variations in conflict dynamics, health system capacities and external support availability. These limitations underscore the need for further research to better understand the broader implications of DR-TB management in diverse CE contexts.

Unmet research priorities

Many potential further research studies based on the gaps and needs were identified during the review, which are summarised in box 2.

To optimise DR-TB management in CE, the cumulative knowledge and experience gained through WHO's technical assistance on DR-TB could be systematically analysed and compared. Emerging practices, such as the rapid adoption of shorter regimens like BPaLM, mass

Box 2 Potential further studies in drug-resistant tuberculosis (DR-TB) management in complex emergency (CE)

1. Analysis and publication of observational studies and country cohorts/Non-Governmental Organization (NGO) experiences, including the historical series of regional Green Light Committee reports from the different WHO regions.
2. Prevalence, outcomes and yield of DR-TB interventions in prisons and internally displaced populations (IDPs) from field working NGOs.
3. Consideration for specific drug-susceptible and DR-TB guidelines adaptations in CE, including approach to prisons, children and IDPs
4. Update the burden of drug-susceptible TB in complex emergencies, exercise not done since 2012,[6] comprising DR-TB and also neglected populations like IDPs, prisons, refugees, etc.
5. The quick adaptation of the Ukraine National TB Programme to war circumstances might be worth reviewing; counting the analysis of BPaLM cohorts (short-term and long-term outcomes including impact in Bedaquiline resistance) and other solutions implemented (eg, decentralisation, use of mobile phone apps, distance monitoring, patient-centred approaches, etc) that could be helpful even in countries not in conflict.
6. Modelling methodologies: Provided the difficulties for operational research in CE, modelling could bring more light to infer adequate approaches or long-term consequences, even for third countries of not acting in potential DR-TB hot spots in CE, like prisons, IDPs, etc. Modelling could benefit from the potential implications and consequences of CE in the efforts towards TB elimination and transboundary policies.
7. Cost-effectiveness studies may contribute to understanding the real value and impact of supporting countries and poor communities in DR-TB, maybe preventing future DR-TB epidemics or impacting the country's economy and restoring national capacities.
8. Identification of minimum packages of interventions and trial outreach and mobile approaches to DR-TB based on new ultraportable diagnostic technologies (eg, chest X-ray, ECG, lateral flow urine lipoarabinomannan assay (LF-LAM), saliva swabs), short treatments and monitoring by smartphone apps.
9. As for similarities in HIV, in the future, the use of long-acting medication in tuberculosis preventive treatment or TB management could be key in outreach and CE-affected populations.

screening in prisons and IDP camps, the use of NAATs, ultraportable CXRs and runaway kits, should be further explored and tested.

These successful experiences could inform the development of tailored manuals or the adaptation of existing DR-TB guidelines to the realities of CE. It is worth remarking that the important changes and updates carried out by Ukraine to optimise DR-TB management are worth exploring and analysing for the benefit of NTPs, even if not immersed in CE.

Additionally, a deeper understanding of the actual burden of DR-TB among IDPs, incarcerated and other populations is critical for effective resistance control.

Currently, no cost-effectiveness studies addressing DR-TB in CE settings have been identified. Combining such studies with modelling approaches could provide valuable insights into the yield of various interventions, the disease burden and the financial challenges associated with DR-TB in CE.

Modelling and cost-effectiveness studies can guide resource allocation by quantifying the benefits of early diagnosis, optimal treatment regimens and integrated service delivery, providing compelling evidence for sustained investment and the consequences of inaction in global AMR or third countries impacted.

Future research should also explore the intersections of climate change, natural disasters and DR-TB. Understanding these dynamics is essential for preparing for and addressing the compounded challenges posed by these global phenomena.

Forthcoming advances like swab tests[97] and long-life anti-TB formulations could be critical in health system disrupted countries. The increasing burden of protracted conflicts and the described intrinsic links between CE and DR-TB, with important limitations on its diagnosis and management, present TB vaccines as an even greater priority.[98]

CONCLUSIONS

The overall burden of DR-TB and its mortality in CE remains largely unknown, as evidence is minimal. This review identified numerous risk factors for DR-TB that are highly prevalent in CE, contributing to the creation of an evidence baseline. Modern warfare significantly alters TB dynamics, presenting multiple known risk factors that amplify resistance. As with other bacterial diseases,[78] the rise of DR-TB can be considered part of the devastating legacy of war.

Countries affected by CE rely heavily on external funding for DR-TB management. Funding and implementing agencies have been crucial in maintaining, updating and restoring DR-TB services, particularly in protracted conflicts. However, diagnosis remains the most critical barrier to accessing care. Despite significant health system disruption and the complexities inherent to CE, countries have demonstrated the capacity to deliver proper care to the limited number of cases diagnosed.

Innovations in diagnosis and treatment have made DR-TB management more feasible, even in settings with severely compromised health systems. However, information on the management of highly vulnerable populations, such as IDPs, children and prisoners, is severely lacking. The circumstances in prisons may be fuelling the DR-TB epidemic in CE communities.

Based on the findings of this review and related literature, we propose priorities and actionable suggestions to address DR-TB in CE. These recommendations are subject to significant limitations due to the scarcity of robust data. Expanding the body of evidence on DR-TB in CE is essential for optimising management strategies and reducing transmission.

Financing DR-TB care in CE is undoubtedly challenging. Inaction will ballast or undermine future efforts towards TB elimination in CE-affected and third

countries, even decades after conflict stabilisation, and exacerbate the global AMR crisis. There is an urgent need to mobilise international efforts to prioritise TB and DR-TB in war and CE contexts.

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